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(54) DEVICES FOR PRESENTING AIRBORNE MATERIALS TO THE NOSE

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(58) Field of Search 347/2, 83; 604/28; 424/1.13; 702/45; 222/160; 128/203.11, 203.12, 200.14

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(57) **ABSTRACT**

An ink-jet dispenser for the micro-dispensation of airborne materials into an individual's airspace for inhalation or sniffing. The ink-jet dispenser will allow the study of temporal integration times, inter-nostril summation, backwards and forwards masking, and other olfactory phenomena.

46 Claims, 25 Drawing Sheets

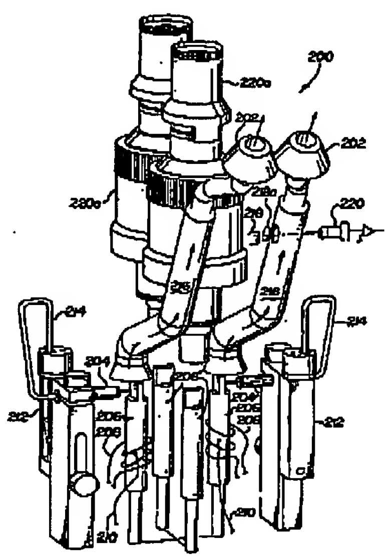

FIG. 21 is a plot of threshold data using an ink-jet-based digital dispenser according to the present invention;

FIG. 22 is a schematic view of a long and short duration olfactory stimulus from an ink-jet based digital dispenser according to the present invention;

FIG. 23A is a schematic view of microreservoirs and manifolds attached to six parallel ink-jet channels;

FIG. 23B is a schematic view of an upper layer of a laser etched plate forming manifolds for the ink-jet channels shown in FIG. 23A;

FIG. 23C is a schematic view of a lower layer of a laser etched plate forming reservoirs for the ink-jet channels shown in FIG. 23A;

FIG. 24 shows human subject threshold tests for left, right and left and right combined nostrils conducted on the ink-jet-based digital dispenser illustrated schematically in FIGS. 3A and 3B;

FIG. 25 shows human subject threshold tests for left, right and left and right combined nostrils conducted on the ink-jet-based digital dispenser illustrated schematically in FIGS. 3A and 3B;

FIG. 26 is a schematic view of the dispersion of an olfactant in an airtube; and

FIG. 27 is a graph of the concentration of an olfactant versus time at 0.005 m from the source of the olfactant.

DESCRIPTION OF THE PREFERRED EMBODIMENT

As shown schematically in FIGS. 1A and 1B, the digital dispenser 10 of the present invention includes ink-jet micro-dispenser technology by incorporating piezoelectric transducer jets 12 which may be formed of piezoelectric material such as lead zirconate titanate (PZT). Those of ordinary skill in the art will recognize, however, that the piezoelectric transducer can be replaced by other transducers such as electrostrictive transducers, magnetostrictive transducers and electromechanical transducers. As shown in FIG. 1B, the digital dispenser 10 preferably includes eight piezoelectric microdispensing channels 12.

The test substances may be dispensed from reservoirs 16 in which test substance volume dispensing resolution preferably will be in the range of 200 picoliters. The test substances may include drugs, fragrances and volatile component containing substances. The test substances may also include nicotine for use in a cigarette withdrawal regimen.

The piezoelectric microdispensers 12 are integrated into individual, modular mechanical and hydraulic assemblies. These assemblies in turn are integrated into the airborne material delivery system. Conventional control electronics 14 and software design well known to those of ordinary skill in the art for use in solder microdispensing are used in the digital dispenser 10. The digital dispenser 10 according to the present invention permits the optimization of microdispenser operating parameters in terms of waveform and frequency for the airborne material/vehicle combinations.

According to a preferred embodiment of the present invention, water, ethanol and propylene glycol are used as the fluid vehicles for low concentration airborne material dispensing. All the test substances of interest are soluble in water, ethanol or propylene glycol, and none of the vehicles will interfere with olfactory thresholds for the 10 to 1000 picoliter dispensing volumes employed by the digital dispenser 10 of the present invention. The surface tensions and viscosities (magnitude and Newtonian vs. non-Newtonian) of the pure test substance solutions to be used are within the range such that their dispensing performance will be acceptable.

A schematic of the functional elements of the micro-dispensing device 12 of the digital dispenser 10 of the present invention is shown in FIG. 1C. As shown in FIG. 1C, the micro-dispensing device 12 incorporated in the device of the present invention includes a fluid fitting 18, a piezoelectric crystal 20, a glass tube 22 and an orifice nozzle 24. The fabrication technology and processes as well as the operating characteristics of this type of device are disclosed and claimed in U.S. Pat. Nos. 5,227,813, 5,235,352, 5,334,415, 5,345,256, 5,365,645, 5,373,314, 5,400,064, 5,402,162, 5,406,319,, 5,414,916, 5,426,455, 5,430,470, 5,433,809, 5,435,060, 5,436,648 and 5,444,467, the entire disclosures of which are hereby incorporated herein by reference. The functional elements of the micro-dispensing device 12 of the digital dispenser 10 of the present invention as shown in FIG. 1C are integrated into a housing 26 that includes a fluid fitting as shown in FIG. 1A. This assembly is installed into a mechanical assembly that includes an electrical connector, fluid reservoir 16, and fluid filter. It also provides the mechanical reference surfaces for mating with the digital dispenser 10 of the present invention.

Airflow in the direction of the arrows shown in FIG. 1A is passive and is controlled by a subject's sniff or inhalation. The interface 28 to a subject preferably is similar to the output of a nasal inhaler, with one output for each nostril, although the interface may also have a single output for both nostrils. The total air volume for each channel preferably is less than 200 ml to insure that all of the airborne material is inhaled during a sniff (average of 0.5 liter/second flow rate during a 0.5 second sniff). Preferably a fan (not shown) and an activated charcoal filter 32 will be attached to the inlet 34 of the device 10 to provide a brief air purge to remove any residual test substance from the system between trials.

The dispensers 12 are targeted onto heated screens 36, preferably formed of platinum, to vaporize the test substance and vehicle. Preferably the platinum screens 36 are heated during the air purge between trials. A water dispenser 30 can be activated to humidify the air. Also, it is preferred that two heated platinum screens 36 are used to allow binasal testing.

If required, an aerosol blocking filter 38 may be included to filter aerosol particles (larger than 1 μm) that might be generated during high frequency multiple droplet dispensing events, due to later droplets impacting into a pool.

In a preferred embodiment, the digital dispenser 10 includes eight droplet generators. Each micro-dispensing device 12 is evaluated in a test stand with isopropanol being used as a test fluid. Droplet size and velocity as a function of drive voltage and frequency are measured for several frequencies. Droplet velocity is measured by stroboscopically "freezing" the drops in space and measuring the droplet-to-droplet distance ($V=f\lambda$) through a microscope. Drop size is measured by measuring the flow rate of the drop stream over a precise time interval.

Each test substance/vehicle solution of interest is tested for its microdispensing performance in the test stand over a range of concentrations. For threshold testing of the sense of smell, 3–4 orders of magnitude dynamic range (60–80 decismels), where:

$$1 \text{ decismel} = \frac{\log 10 \text{ [odor concentration]}}{20}$$

are needed. This is achieved by a combination of varying the concentration of the test substance in the vehicle and varying the amount dispensed. For example, the delivered mass requirements of one olfactory stimulation could require